REMARKS

Claims 28, 29, 31, and 32 are pending. Claim 44 has been added. Claims 28, 29, 31, 32 and 44-47 are presented for further consideration.

The cross-reference to related applications has been corrected as requested.

Claims 28, 29, 31, and 32 are rejected under Section 102(b) based on Harris *et al.* (WO 94/09136, published 4/28/1994). Forwarded with this response is a Rule 131 declaration of Dr. Hans Hansen, one of the inventors. Dr. Leung no longer is employed by Immunomedics. Applicant has sent the Rule 131 declaration to Dr. Leung's attorneys, who have forwarded it on to Dr. Leung for signature. However, Dr. Leung has not yet returned his executed declaration.

Included with the Rule 131 declaration is a copy of a monthly progress report *submitted* by Dr. Leung while he was employed by Immunomedics, Inc. The date on the monthly progress report has been redacted, but was before April 28, 1994. The report discusses experiments performed on chimeric LL2, humanized LL2.1 (HuLL2) and humanized LL2.2 (mutHuLL2). The chimeric and humanized LL2 antibodies of the progress report are those described in the present application.

Also attached to the Rule 131 declaration is a copy of a page from Dr. Leung's Immunomedics lab notebook entitled "DNA Sequence of LL2 Gamma Chain Variable Region as Cloned Out Using CHIA and VH1Back Primers in a PCR Reaction," recording work done at Immunomedics. The date on the laboratory notebook page has been redacted, but was before April 28, 1994. The page from the laboratory notebook shows sequence comparison of the LL2 heavy chain to three of the most commonly used human heavy chain frameworks for CDR grafting at the time. They were, namely, EU, NEW and KOL. A summary on the number of amino acid mismatches to the corresponding FR1, FR2 and FR3 of murine LL2 heavy chain was listed. It indicates at the bottom EU framework matches better with LL2. Looking at the left of the start of the murine LL2 sequence, there are hand written residues. Those which differ for NEWM are hand written above, and those that differ for KOL are written below, the murine LL2 amino acid sequence. Those positions where the EU sequence amino acids differ from the murine LL2 sequence are written between the nucleotide sequences. In FR4 the first three critical amino acid residues of murine LL2 are WGQ. The amino acid residues of EU at corresponding positions are EYN, and therefore, regardless of its best overall homology, choosing the whole EU framework for CDR-grafting was not a good choice. It was then rationalized that FR4 did not necessarily have

to come from the same human heavy chain. Both NEWM and KOL were a better fit for FR4 than EU because they have fewer residues that differ and because the first three critical residues are the same as those in the murine framework.

The Rule 131 declaration with the appended evidence shows that applicant had reduced the present invention to practice prior to the effective date of the cited Harris document. Accordingly, the rejection based on Harris is moot.

In the Decision on Appeal, the Board agreed with applicant that "the LL2 monoclonal antibody was used in the Specification to exemplify the claimed method, not to limit the scope of the claimed invention." Accordingly, applicant now submits claim 44-47. The scope of claim 44 is consistent with the holding of the Board that the LL2 monoclonal antibody exemplifies a method of designing amino acid sequences of variable domains of a humanized monoclonal antibody, and provided adequate written support for more than humanization of the LL2 monoclonal antibody.

If there are any problems with this response, or if the examiner believes that a telephone interview would advance the prosecution of the present application, Applicant's attorney would appreciate a telephone call. In view of the foregoing, it is believed none of the references, taken singly or in combination, disclose the claimed invention. Accordingly, this application is believed to be in condition for allowance, the notice of which is respectfully requested.

Respectfully submitted,

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DATE

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